

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.: 37945-0018

| | | |
|----------------|--|------------------------|
| Applicants(s): | Angus George DALGLEISH <i>et al.</i> | Confirmation No.: 6462 |
| Appl. No.: | 09/857,691 | Examiner: M. Davis |
| Filing Date: | September 5, 2001 | Group Art Unit: 1642 |
| Title: | USE OF HUMAN PROSTATE CELL LINES IN CANCER TREATMENT | |

DECLARATION OF JONATHAN MARK DAVIES

I, Jonathan Mark Davies, do hereby declare as follows:

I hold a D.Phil. Degree in Pharmacology and Physiology from Oxford University (United Kingdom).

I am a Chartered Patent Attorney having been entered on the Register of Patent Attorneys in the United Kingdom in 1986.

I am a Fellow of the Chartered Institute of Patent Attorneys (UK).

I am a qualified European Patent Attorney having been entered on the List of Professional Representatives before the European Patent Office in 1987.

I am a member of the European Patents Institute.

By virtue of my qualifications and my experience in practice as a European Patent Attorney, I am familiar with and fully conversant with the provisions of the European Patent Convention (EPC) which governs the filing, prosecution and grant of European Patents.

I have been asked to provide a Declaration in support of US Patent Application No. 09/857,691 "Use Of Human Prostate Cell Lines In Cancer Treatment".

I am the Patent Attorney principally responsible for the drafting of this application. The US attorney of record (John P. Isacson, Reg No. 33,715) is responsible for prosecuting this application before the US Patent and Trade Mark Office, on my instructions.

This Declaration addresses the availability to the public of a sample of the cell line 1542-CP3TX-CRL-12037 which was deposited with ATCC under Accession Number CRL-12037, February 23rd 1996.

The deposit was made in the name of Suzanne L. Topalian.

The deposited material was placed in the American Type Culture Collection (ATCC) under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure. The ATCC issued a receipt for the original deposit pursuant to Rule 7.3 of the Budapest Treaty and also issued a viability statement pursuant to Rule 10.2 of the Budapest Treaty.

The ATCC is recognised as an International Depository Authority (IDA) for the purposes of the Budapest Treaty. According to the Regulations of the Budapest Treaty, any micro-organism deposited with an IDA shall be stored by the authority, with all the care necessary to keep it viable and uncontaminated, for a period of at least five years after the most recent request for the furnishing of a sample of the deposited micro-organisms was received by the said authority and, in any case, for a period of at least thirty years from the date of the deposit. (Rule 9.1).

Rule 11.3 regulates the furnishing of samples to parties legally entitled. It states as follows:

- (a) Any IDA shall furnish a sample of any deposited micro-organism to any authority, natural person or legal entity (hereinafter referred to as “the certified party”), on the request of such party, provided that the request is made on a form whose contents are fixed by the Assembly and that on the said form the Industrial Property Office certifies:
 - (i) That an application referring to the deposit of the micro-organism has been filed with that office for the grant of a patent and that the subject matter of the application involves the said micro-organism or the use thereof;
 - (ii) That, except where the second phrase of (iii) applies, publication for the purposes of patent procedure has been effected by that office;
 - (iii) Either that the certified party has a right to a sample of the micro-organism under the law governing patent procedures before that office and, where the said law makes the said right dependent on the fulfilment of certain conditions, that that office is satisfied that such conditions have actually been fulfilled or that the certified party has affixed his signature on a form before that office and that, as a consequence of the signature of the said form, the conditions for furnishing a sample to the certified party are deemed to be fulfilled in accordance with the law governing patent procedure before that office; where the certified party has the aid right under the said law prior to publication for the purposes of patent procedure by the said office and such publication has not yet been affected, the certification shall expressly state so and shall indicate, by citing it in the customary manner, the applicable provision of the said law, including any Court decision.

The micro-organism in question in the current situation is the deposited cell line NIH1542-CP3TX. European Patent Application No. 97904061 filed on 30th January 1997 by the US Government (NIH) involves this deposited micro-organism material and the use thereof. The European application is based on an International application published as WO97/28255. The European application issued as published European Patent No. EP 0877798 B1 which was granted on 7th May 2003.

In my expert opinion the deposited cell line satisfies all of the requirements of a Budapest Treaty Deposit of a Micro-organism for the Purposes of Patent Procedure.

The deposit and release of biological material under the EPC is governed mainly by Rule 28 EPC. Rule 28 (3) states as follows:

- “(3) The deposited biological material shall be available upon request to any person from the date of publication of the European patent application and to any person having the right to inspect the files pursuant to Article 128, paragraph 2, prior to that date. Subject to paragraph 4, such availability shall be effected by the issue of a sample of the biological material to the person making the request (hereinafter referred to as “the requester”).

Said issue shall be made only if the requester has undertaken vis-à-vis the applicant for or proprietor of the patent not to make the biological material or any biological material derived there from available to any third party and to use that material for experimental purposes only, until such time as the patent application is refused or withdrawn or deemed to be withdrawn, or before the expiry of the patent in the designated state in which it last expires, unless the applicant for or proprietor of the patent expressly waives such an undertaking.

The Undertaking to use the biological material for experimental purposes only shall not apply in so far as the requester is using the material under a compulsory licence. The term “compulsory licence” shall be construed as including ex officio licenses and the right to use patented inventions in the public interest”.

The steps to be taken to obtain a sample of a deposited biological material are governed by EPC Rule 28 (7) which reads as follows:

- “(7) The request provided for in paragraph 3 shall be submitted to the European Patent Office on a form recognised by that office. The European Patent Office shall certify on the form that a European patent application referring to the deposit of the biological material has been filed, and that the requester or the expert nominated by him is entitled to the issue of a sample of that material. After grant of the European patent, the request shall also be submitted to the European Patent Office.”

EPC Rule 28 (8) states that the European Patent Office (EPO) shall transmit a copy of the request, with the certification provided for in paragraph 7, to the depository institution as well as to the applicant for or the proprietor of the patent.

In my expert opinion the provisions of the EPC relating to availability of deposited material from the ATCC deposit CRL-12037 have been met by the publication and subsequent grant of the European application and the European patent involving the cell line.

In my expert opinion a sample of the deposited material is available to any person provided that they make the appropriate request in the appropriate form accompanied by the appropriate undertaking through the European Patent Office.

In my expert opinion the ATCC, as an International Depository Authority under the Budapest Treaty, must provide a sample of deposited material to a suitably certified person. The correctness of my expert opinion is demonstrated by the events described below.

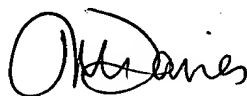
On December 10, 2004, the EPO issued on EPO form 1143a (10.98) (copy attached as Tab 1) a request to the ATCC to provide Onyvax Ltd., as a member of the public, with a sample of deposit no. CRL-12037, among others. This deposit is for NIH1542-CP3TX cells. The deposit is publicly available by virtue of the issuance of EP 0 877 798 B1. As stated on page 2, item 3 of the EPO form:

the certified party has a right to a sample of the microorganism identified in Section I. above under the law governing patent procedure before this Office, and this Office is satisfied that the conditions prescribed by the said law have actually been fulfilled.

Accordingly, deposit no. CRL-12037 (NIH1542-CP3TX cells) are publicly available and a sample must be provided to any requesting member of the public. Here, Onyvax, as a member of the general public, will receive a sample of the deposit in due course.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements and the like are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

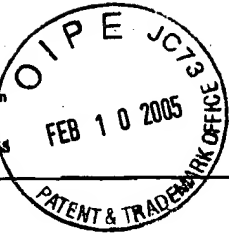
Signed:



Date: 4th Feb 2005
Place: Cambridge
(UK).



CPA/EPO/GEB
D-69296 München
+ 49 89 2339-0
TX 523 656 spm d
FAX + 49 89 2339-4443



Europäisches
Patentamt

European
Patent Office

Office européen
des brevets

Generaldirektion 2

Direction Générale 2

Direction Générale 2

Dr. A. Walker, CEO
Onyvax Limited
St. George's Hospital Medical School
Granmer Terrace
London SW17 0RE
GRANDE BRETAGNE

Datum/Date

10-12-2004

| | |
|--|---|
| Zeichen/Ref./Ref. | Anmeldung Nr./Application No./Demande n°/Patent Nr./Patent No./Brevet n°. |
| 21-XI | 97904061.5-2405/PCT/US9701430 |
| Anmelder/Applicant/Demandeur/Propriétaire/Proprietario/Titulaire | |
| THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, | |

Please find enclosed a copy of your request for the furnishing of a sample of the deposited biological material. The original has been forwarded to the depositary institution and a copy of it to the applicant.

Under Rule 12.1(a)(iv) of the Budapest Treaty, the depositary institutions are entitled to charge a fee for the issuance of samples. The fee shall be paid by the requester direct to the relevant institution. The schedules of fees charged by the depositary institutions are published in the WIPO publications "Intellectual Property" and "Guide to the deposit of micro-organisms under the Budapest Treaty" as well as in the Official Journal of the European Patent Office.

RECEIVING SECTION



Antrag auf Abgabe von Proben
hinterlegter Mikroorganismen
(Bestätigung des Antrags durch
Europäische Patentamt)

Request for the furnishing of sam-
ples of deposited microorganisms
(certification of the request by the
European Patent Office)

Requête en remise d'échantillons
de micro-organismes déposés
(certification de la requête par
l'Office européen des brevets)

Budapester Vertrag über die
internationale Anerkennung der
Hinterlegung von Mikroorganismen für
die Zwecke von Patentverfahren

Budapest Treaty on the international
recognition of the deposit of micro-
organisms for the purposes of patent
procedure

Traité de Budapest sur la reconnais-
sance internationale du dépôt des
micro-organismes aux fins de la
procédure en matière de brevets

• Regel 11.3 a) des Budapester Vertrags in
Verbindung mit Regel 28 EPU

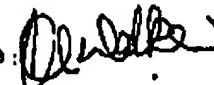
• Rule 11.3(a) of the Budapest Treaty in
conjunction with Rule 28 EPC

• Règle 11.3a) du Traité de Budapest
ensemble la règle 28 CBE

Bilaterale Abkommen
• Regel 28 EPU

Bilateral agreements
• Rule 28 EPC

Accords bilatéraux
• Règle 28 CBE

| | | |
|--|--|--|
| EMPFÄNGER (Name und Anschrift der internationalen Hinterlegungsstelle) | TO (Name and address of international depository authority) American Type Culture Collection 12301 Parklawn Drive Rockville MD 20852 USA | DESTINATAIRE (Nom et adresse de l'autorité internationale de dépôt) |
| Der Unterzeichnete beantragt die Abgabe einer Probe des nachstehend bezeichneten Mikroorganismus gemäß: • Regel 11.3a) der Ausführungsordnung zum Budapest Vertrag oder • Nummer 23 des bilateralen Abkom- mens | The undersigned hereby requests the furnishing of a sample of the micro- organism identified hereunder: • in accordance with Rule 11.3(a) of the Regulations under the Budapest Treaty, or • point 23 of the bilateral agreement | Le soussigné demande la remise d'un échantillon du micro-organisme identifié ci-après conformément: • à la règle 11.3a) du règlement - d'exécution du Traité de Budapest, ou • au point 23 de l'accord bilatéral |
| I. Kennzeichnung des Mikroorganismus / Identification of the microorganism / Identification du micro-organisme Eingangsnummer der Hinterlegung: Accession number of the deposit: CRL-12037, CRL-12264, CRL-12265, CRL-12266 Numéro d'ordre du dépôt: | | |
| II. Patentmeldung oder Patent, das/dies auf den hinterlegten Mikroorganismus Bezug nimmt Patent application or patent referring to the microorganism deposited Demande de brevet ou brevet faisant état du micro-organisme déposé <input checked="" type="checkbox"/> Europäische Patentanmeldung Nr.: European patent application No.: 97904061 Demande de brevet européen n°: eingereicht am: von: filed on: 30 Jan 1997 by: US Government (NIH) déposée le: par: <input checked="" type="checkbox"/> Internationale (PCT) Anmeldung Nr.: International (PCT) application No.: WO 97/26255 Demande internationale (PCT) n°: <input checked="" type="checkbox"/> Europäisches Patent Nr.: European patent No.: EP 0 877 798 B1 Brevet européen n°: erteilt am: an: granted on: 07 May 03 to: US Government (NIH) délivré le: à: | | |
| III. Antrag auf Angaben / Request for information / Demande d'informations Der Unterzeichnete / The undersigned / Le soussigné <input checked="" type="checkbox"/> beantragt / requests / demande <input type="checkbox"/> beantragt nicht / does not request / ne demande pas daß die Bedingungen angegeben werden, unter denen der Mikroorganismus von der internationalen Hinterlegungsstelle gezüchtet und aufbewahrt worden ist. an indication of the conditions which the international depository authority employs for the cultivation and storage of the microorganism. l'indication des conditions utilisées par l'autorité de dépôt internationale pour cultiver et conserver le micro-organisme. | | |
| IV. Bestätigte Partei / Certified party / Partie certifiée Name / Nom: Dr. Anthony Walker Datum / Date: 11 November 2004 Anschrift / Address / Adresse: Onyx Limited St. George's Hospital Medical School Cranmer Terrace London SW17 0RE Unterschrift / Signature:  | | |

Bestätigung

Certification

Certification

Es wird bestätigt:

It is hereby certified that:

Il est certifié :

1. daß die/das unter II. genannte Patent-anmeldung/Patent, die/das auf die Hinterlegung des unter I. bezeichneten Mikroorganismus Bezug nimmt

1. the patent application/patent specified under Section II. above referring to the deposit of the microorganism identified under Section I. above

1. que la demande de brevet/le brevet indiqué sous chiffre II., faisant état du micro-organisme identifié sous chiffre I.

☐ bei diesem Amt eingereicht worden ist;

☒ has been filed with this Office;

☐ a été déposée auprès du présent Office;

☐ mindestens einen Vertragssatz zum Zweck der Erteilung eines europäischen Patents bestimmt, der Vertragssatz des PCT ist, für den dieses Amt „Bestimmungsamt“ im Sinne des genannten Vertrags ist;

☒ designates for the grant of a European patent at least one State party to the PCT for which this Office is the "designated Office" within the meaning of the said Treaty;

☐ désigne, en vue de la délivrance d'un brevet européen, au moins un Etat partie au PCT pour lequel le présent Office est «office désigné»;

☐ von diesem Amt erteilt worden ist;

☒ has been granted by this Office;

☐ a été délivré par le présent Office;

und daß ihr/sein Gegenstand sich auf den genannten Mikroorganismus bezieht.

and its subject matter involves the said microorganism or the use thereof.

et quo son objet se rapporte audit micro-organisme ou à son utilisation.

2. ☐ daß eine Veröffentlichung für Zwecke des Patentverfahrens stattgefunden hat

2. ☒ publication for the purpose of patent procedure has been effected

2. ☐ qu'une publication aux fins de la procédure en matière de brevets a été faite

☐ durch dieses Amt;

☒ by this office;

☐ par le présent Office;

☐ durch das Internationale Büro der WIPO als Internationale Veröffentlichung nach dem PCT;

☒ by the international Bureau of WIPO as an international publication under the PCT;

☐ par le Bureau International de L'OMPI en tant que publication internationale en vertu du PCT;

oder

or

ou

- ☐ daß die bestätigte Partei nach Regel 28 (3), Satz 1 in Verbindung mit Artikel 128 (2) des Europäischen Patentübereinkommens Anspruch auf Abgabe einer Probe vor der Veröffentlichung hat.

- ☐ the certified party has a right to a sample before publication under Rule 28 (3), first sentence, in conjunction with Article 128 (2) of the European Patent Convention.

- ☐ que la partie certifiée a droit à un échantillon avant la publication en vertu de la règle 28 (3), première phrase, ensemble l'article 128 (2) de la Convention sur le brevet européen.

3. daß die bestätigte Partei nach dem für das Patentverfahren vor diesem Amt geltenden Recht Anspruch auf eine Probe des unter I. bezeichneten Mikroorganismus hat und daß sich dieses Amt davon überzeugt hat, daß die für die Abgabe einer derartigen Probe rechtlich vorgeschriebenen Bedingungen erfüllt sind.

3. the certified party has a right to a sample of the microorganism identified in Section I. above under the law governing patent procedure before this Office, and this Office is satisfied that the conditions prescribed by the said law have actually been fulfilled.

3. que la partie certifiée a droit à un échantillon du micro-organisme identifié sous chiffre I., en vertu du droit qui régit la procédure en matière de brevets devant le présent Office, et que le présent Office s'est assuré que les conditions prescrites par ledit droit pour la remise d'un tel échantillon sont effectivement remplies.

4. ☐ daß die vorstehende Bestätigung eine Hinterlegung nach einem bilateralen Abkommen betrifft

4. ☐ that the above certification concerns a deposit pursuant to a bilateral agreement

4. ☐ que la présente certification s'applique à un dépôt selon un accord bilatéral

Europäisches Patentamt / European Patent Office / Office européen des brevets

Datum / Date: 07.12.04

W. Claessens

Unterschrift / Signature

**Erklärung zur Anforderung einer
Probe eines hinterlegten
Mikroorganismus**

Regel 28 (3) des Europäischen Patentüberein-
kommens

Diese Erklärung ist dem Antrag auf
Abgabe einer Probe des nachstehend
bezeichneten hinterlegten
Mikroorganismus beigelegt:

**Declaration for the purpose of
obtaining a sample of a deposited
microorganism**

Rule 28 (3) of the European Patent Convention

This declaration accompanies the
request for furnishing of a sample of
the deposited microorganism identi-
fied hereunder:

**Déclaration en vue de l'obtention
d'un échantillon de
micro-organisme déposé**

Règle 28 (3) de la Convention sur le brevet
européen

La présente déclaration accompagne la
requête en remise d'un échantillon du
micro-organisme déposé identifié ci-
après :

| | | |
|---|--|---------------------------------------|
| I. Kennzeichnung des Mikroorganismus / Identification of the microorganism / Identification du micro-organisme Eingangsnummer der Hinterlegung: Accession number of the deposit: CRL-12037, CRL-12040, CRL-12264, CRL-12265 Numéro d'ordre du dépôt : | | |
| Hinterlegungsstelle: Depositary authority: American Type Culture Collection Autorité de dépôt : | | |
| II. Patentmeldung oder Patent, die/das auf den hinterlegten Mikroorganismus Bezug nimmt Patent application or patent referring to the microorganism deposited Demande de brevet ou brevet faisant état du micro-organisme déposé | | |
| <input checked="" type="checkbox"/> Europäische Patentanmeldung Nr.: European patent application No.: 97804061 Demande de brevet européen n° : | eingereicht am: filed on: 30 Jan 1997 | von: by: US Government (NIH) |
| <input checked="" type="checkbox"/> Internationale (PCT) Anmeldung Nr.: International (PCT) application No.: WO 97/28255 Demande internationale (PCT) n° : | déposée le : | par : |
| <input checked="" type="checkbox"/> Europäisches Patent Nr.: European patent No.: EP 0 877 798 B1 Brevet européen n° : | erteilt am: granted on: 07 May 03 délivré le : | an: to: US Government (NIH) à : |

Der Unterzeichnete, der im Antrag und
nachstehend als bestätigte Partei
genannt ist, verpflichtet sich gegenüber
dem unter II. genannten Anmelder oder
Patentinhaber:

- die erhaltene Probe der Kultur des
unter I. bezeichneten Mikroorganismus
oder eine davon abgeleitete Kultur
Dritten nicht zugänglich zu machen,
bevor die unter II. genannte Patentan-
meldung zurückgewiesen oder
zurückgenommen wird oder als
zurückgenommen gilt oder das auf
diese Anmeldung erteilte europäische
Patent in allen benannten Vertrags-
staaten erloschen ist;
- diese Probe oder eine davon abgeleitete
Kultur bis zu dem Zeitpunkt, zu dem die
unter II. genannte Patentanmeldung
zurückgewiesen oder zurückgenommen
wird oder als zurückgenommen gilt, oder
bis zum Zeitpunkt der Bekanntmachung
des Hinweises auf die Erteilung des
europäischen Patents lediglich zu
Versuchszwecken zu verwenden ☺.

The undersigned, identified in the
request and hereunder as the certified
party, undertake: vis-à-vis the appli-
cant for or proprietor of the patent
referred to under section II:

- not to make the furnished sample of
the culture of the microorganism
identified under Section I. or any
culture derived therefrom available to
any third party ☺ before the patent
application identified under Section II.
has been refused or withdrawn or is
deemed to be withdrawn or before the
expiry of the European patent granted
on the basis of that application in the
designated State in which it last
expires;
- to use the said sample or a culture
derived therefrom for experimental
purposes only, until such time as the
patent application identified under
Section II. is refused or withdrawn or is
deemed to be withdrawn or until the
date of publication of the mention of
the grant of the European patent ☺.

Le soussigné, identifié dans la requête
et ci-dessous en tant que partie
certifiée, s'engage à l'égard du
demandeur ou du titulaire du brevet
visé sous II:

- à ne pas communiquer à des tiers ☺
l'échantillon obtenu de la culture du
micro-organisme identifié sous I. ou
une culture qui en est dérivée avant
que la demande de brevet identifiée
sous II. ait été rejetée ou retirée ou soit
réputée retirée ou que le brevet
européen délivré sur la base de cette
demande s'éteigne dans tout les Etats
contractants désignés ;
- à n'utiliser ledit échantillon ou une
culture qui en est dérivée qu'à des fins
expérimentales jusqu'à la date à
laquelle la demande de brevet identi-
fiée sous II., ait été rejetée ou retirée
ou soit réputée retirée ou jusqu'à la
date de la publication de la mention de
la délivrance du brevet européen ☺.

III. Bestätigte Partei / Certified party / Partie certifiée
Name / Nom : Dr. Anthony Walker

Datum / Date : 11 November 2004

Anschrift / Address / Adresse :

Onyx Limited
St. George's Hospital Medical School
Cranmer Terrace
London SW17 0RE

Unterschrift / Signature :

